REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and the following remarks.

I. Status of the Claims

Claims 38, 40, 44-53, 55-56 and 59 are currently pending in the application, with claim 38 being the independent claim. Claims 39, 41-43, 57-58, 60 and 64-66 are canceled without prejudice to or disclaimer of the subject matter therein. Claims 1-37, 54 and 61-63 were previously canceled.

II. The Amendments to the Claims

Claim 38 is amended to recite that the first polypeptide comprises at least one of an epitope, a functional domain of a protein, a structural domain of a protein, a mutated variant of a protein or a truncated variant of a protein, and the protein is derived from a pathogen. Further, claim 38 is amended to specify that the second polypeptide is SV40 large T-antigen and the chaperone belongs to the family of heat shock protein (hsp) 70 chaperone. Support for the amendments to claim 38 may be found throughout the specification and in particular at page 19, lines 18-20, in original claims 3, 4 and 10 and in claims 39 and 42 as previously presented.

Claims 44-46 are amended to correct claim dependency.

These amendments do not introduce any new matter into the application. The claims have been amended to address the concerns raised in the Office Action with regard to patentable subject matter, and place the application in condition for allowance or, at least, in better condition for appeal. Entry of these amendments after final is therefore respectfully requested.

III. The Rejection Under 35 U.S.C. § 112, First Paragraph

The Office Action, at pages 2-3, rejects claims 58 and 64-66 under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which is pertains or with which it is most nearly connected, to use the invention commensurate in scope with the claims. Specifically, the Office Action contends that the specification does not reasonably provide enablement for any unstable polypeptide or any tag that are encompassed by the claims. Further, the Office Action maintains that the specification, while showing an immune response in mice, allegedly fails to show that the vectors described in the present invention will induce a vaccine immune response in humans with the range of antigens allowed by the claims. Applicants respectfully traverse this ground of rejection.

The M.P.E.P., section § 2164.08, states the following with regard to enablement commensurate in scope with the claims:

> The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation'." *In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)*. Nevertheless, not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991)*. All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. *See, e.g., In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)*.

With regard to the breadth of a claim, the M.P.E.P. states:

> As concerns the breadth of a claim relevant to enablement, the only relevant concern should be whether the scope of enablement provided to one skilled in the art by the disclosure is commensurate with the scope of protection sought by the claims. *In re Moore, 439 F.2d 1232, 1236, 169 USPQ 236, 239 (CCPA 1971)*.

Nevertheless, solely to advance prosecution, and not in acquiescence with the propriety of the rejection, the foregoing cancels claims 57-58, 60 and 64-66, and amend claim 38 to recite a polynucleotide encoding a stable fusion protein comprising a first (poly)peptide which is unstable in a cell comprising at least one of an epitope of a protein, a functional domain of a protein, a structural domain of a protein, a mutated variant of a protein or a truncated variant of a protein, where *the protein is derived from a pathogen,* and a second (poly)peptide *which is SV40 large T-antigen* carrying at least one of an internal deletion or a C-terminal deletion and co-precipitates with a chaperone that belongs to the family of heat shock protein (hsp) 70 chaperone. Further, claim 50 is directed to a vector comprising the polynucleotide; claim 51 is drawn to a host cell comprising the polynucleotide or the vector; claim 52 is drawn to a method for the production of the fusion protein; claim 55 is directed to a method for the production of the first (poly)peptide; claim 56 is drawn to a method for the production of a complex comprising the fusion protein and the chaperone; and claim 59 is drawn to a kit comprising the polynucleotide, the vector or the host cell.

Thus, the claims as amended are solely directed to polynucleotides encoding fusion proteins comprising specific first and second (poly)peptides, and to the use of these polynucleotides for the recombinant expression of proteins. The amended claims are no longer directed to methods for immunizing a subject.

As explained in detail in the specification, it has been surprisingly discovered that the formation of a stable complex of a chaperone with a (poly)peptide correlates not only with an increased stability of the (poly)peptide but, surprisingly, also with the increased stability of a fusion protein comprising a first (poly)peptide and a second (poly)peptide forming said stable complex with said chaperone. Thus, the polynucleotide of the present invention may advantageously be used to express said fusion protein in a cell to high levels which may exceed 0.1 $\mu g/10^6$ cells (*see* page 7, lines 23-29 in the specification). In fact, when a protein derived from a pathogen, which as such is unstable in a cell, is linked to a SV40 large T-antigen carrying at least one internal or C-terminal deletion, a complex between the protein and the chaperone is

formed, resulting in a fusion protein with increased stability. The increased stability of the fusion protein leads to increased expression of the fusion protein in a host cell, allowing the production of high amounts of fusion protein by the host cell. Since the fusion protein can be cleaved upon its production to yield an isolated protein derived from a pathogen, the use of the polynucleotide according to amended claim 38 enables the production of such unstable proteins in high yields.

The specification provides extensive information to enable the person skilled in the art to produce and/or use polynucleotides of the invention. As disclosed in Example 7, cT1-272/pathogenic antigen-chimeric genes can be obtained that encode a fusion protein comprising the SV40 large T-antigen carrying a C-terminal deletion as a second (poly)peptide and a pathogenic antigen as the first (poly)peptide. These polynucleotides can easily be integrated into a vector according to amended claim 50, which in turn can easily be used to transform a host cell according to claim 51, which again can easily be used for the production of a fusion protein according to claim 52, for the production of a first (poly)peptide according to claim 55, or for the production of a complex according to claim 56. Therefore, the specification does enable any person skilled in the art to make and/or use the invention commensurate in scope with the claimed invention.

Accordingly, the rejection is moot. Reconsideration and withdrawal of this ground of rejection are therefore respectfully requested.

IV. The Rejection Under 35 U.S.C. § 103(a)

The Office Action, at pages 3-4, rejects claims 38-53, 55-56, 59-60 and 64-66 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schirmbeck *et al.* (*Eur. J. Immunol. 27*: 2016 (1997) ("Schirmbeck") and Fu *et al.* (*J. Virol. 67*: 6866-71 (1993)) ("Fu"). The Office Action contends that Schirmbeck teaches two constructs of SV40 Tag associated with hsp73 and alleges that one of ordinary skill in the art would have known that peptides and protein fragments are degraded and that association of hsp73 with Tag is not limited to TAP deficient cells. Further, the Office Action states that Fu shows that chimeric or fusion proteins can be made with

the Tag, and concludes that the claimed invention is allegedly obvious over the cited prior art documents. Applicants respectfully traverse this ground of rejection.

A. Summary of the Claimed Invention

Claim 38, as amended, recites a polynucleotide encoding a *stable* fusion protein comprising a first (poly)peptide which is unstable in a cell comprising at least one of an epitope of a protein, a functional domain of a protein, a structural domain of a protein, a mutated variant of a protein or a truncated variant of a protein, where *the protein is derived from a pathogen,* and a second (poly)peptide which is SV40 large T-antigen carrying at least one of an internal deletion or a C-terminal deletion and co-precipitates with a chaperone that belongs to the family of heat shock protein (hsp) 70 chaperone. Further, claim 50 is directed to a vector comprising the polynucleotide; claim 51 is drawn to a host cell comprising the polynucleotide or the vector; claim 52 is drawn to a method for the production of the fusion protein; claim 55 is directed to a method for the production of the first (poly)peptide; claim 56 is drawn to a method for the production of a complex comprising the fusion protein and the chaperone; and claim 59 is drawn to a kit comprising the polynucleotide, the vector or the host cell.

B. The Cited References Fail to Teach Each and Every Element of the Claimed Invention

Schirmbeck discloses a polynucleotide encoding for the wild type SV40 large T-antigen ("*wtT-Ag*") and polynucleotides encoding for two different, truncated variants of the wild type SV40 large T-antigen (non-karyophilic T-Ag variant "*cT-Ag*" and karyophilic T-Ag-variant "*T272*"). Schirmbeck discloses that the truncated variants, but not the wild type T-antigen, form stable complexes with chaperones like hsp73. However, Schirmbeck et al. fails to teach or suggest preparing a chimeric polynucleotide comprising the DNA-sequence encoding for a truncated variant of the wild type SV40 large T-antigen and a DNA-sequence encoding for a protein derived from a pathogen. Thus, Schirmbeck fails to teach or suggest the claimed invention.

The additional reference, Fu, does not remedy the deficiencies of Schirmbeck. Fu discloses fusion polypeptides obtained by translocating certain cytotoxic T-lymphocyte epitopes (an H-2D^b-restricted SV40 T-antigen site I epitope having a length of 10 amino acids and an H-2K^b-restricted herpes simplex virus glycoprotein B epitope having a length of 7 amino acids) into positions 350 and 650 of the SV40 large antigen. However, the SV40 T-antigen into which the small epitopes are translocated is not a truncated SV40 large T-antigen and therefore does not form stable complexes with chaperones that belong to the hsp70 chaperone family. Thus, Fu, like Schirmbeck, fails to disclose or suggest the claimed invention.

C. There is no Reason to Combine the Known Elements in the Fashion Claimed

Since Fu fails to disclose or suggest stable protein complexes, the person skilled in the art, in view of the teaching of Fu, would have not been able to recognize that the expression of a protein which is unstable can be significantly increased by expressing this protein in the form of a fusion protein wherein the protein is linked to a truncated SV40 large T-antigen. In fact, Fu is absolutely silent about truncated SV40 large T-antigens and is consequently also silent about the formation of stable complexes between the truncated SV40 large T-antigen and chaperones like hsp73. Accordingly, one of ordinary skill in the art would have had no reason to modify the polynucleotides of Schirmbeck by inserting a sequence encoding a polypeptide comprising an epitope, domain or variant of a protein derived from a pathogen, because Fu fails to teach or suggest stable protein complexes.

For at least these reasons, the rejection of the claims under 35 U.S.C. § 103 (a) is improper. Reconsideration and withdrawal of this ground of rejection are therefore respectfully requested.

CONCLUSION

All of the stated grounds of rejection have been properly traversed or rendered moot. Accordingly, the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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